FDA Grants Trastuzumab Deruxtecan Breakthrough Designation for HER2+ NSCLC

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Published: Monday, May 18, 2020

The FDA has granted a breakthrough therapy designation to fam-trastuzumab deruxtecan-nxki (Enhertu) for the treatment of patients with metastatic non–small cell lung cancer (NSCLC) whose tumors have a HER2 mutation and with disease progression on or after platinum-based therapy.[1]

The designation, which will accelerate the development and review of the antibody-drug conjugate (ADC) in this setting, is based on findings from the ongoing phase 2 DESTINY-Lung01 trial, as well as data from a phase 1 trial.[2] In the phase I study, trastuzumab deruxtecan induced an overall response rate (ORR) of 72.7% (n = 8) among 11 patients with HER2-positive NSCLC. The median progression-free survival (PFS) in these patients was 11.3 months (95% CI, 8.1-14.3).

“Today’s news is very welcome as we continue to evaluate the potential of Enhertu to help patients with this devastating type of lung cancer,” José Baselga, MD, PhD, executive vice president, Oncology R&D, AstraZeneca, which co-develops trastuzumab deruxtecan with Daiichi Sankyo, stated in a press release. “Targeted treatments and immunotherapies are demonstrating tremendous advancements, but there remains an unmet medical need for patients with HER2 mutations who are not benefiting from such therapies or for those whose cancer continues to progress.”

The open-label, multicenter, global phase 2 DESTINY-Lung01 trial is evaluating trastuzumab deruxtecan in 170 patients with unresectable and metastatic nonsquamous NSCLC whose cancer has progressed after 1 or more systemic therapies including chemotherapy, molecular targeted therapy, or immunotherapy. The population will comprise 90 patients with HER2-mutant disease and 80 patients with HER2 overexpression, defined as IHC 3+ or IHC 2+. The primary end point is ORR, with secondary end points including duration of response, disease control rate, PFS, and overall survival.

In the press release, AstraZeneca and Daiichi Sankyo reported that the safety and tolerability of trastuzumab deruxtecan in DESTINY-Lung01 has been comparable to what was reported in the phase 1 trial. Thus far, among 42 patients evaluable for safety, the most frequently occurring adverse events have been nausea, alopecia, anemia, decreased appetite, and decreased neutrophil count. Five cases of grade 2 treatment-related interstitial lung disease (ILD) and pneumonitis have been reported. No ILD-related deaths have occurred.

According to AstraZeneca and Daiichi Sankyo, interim data from DESTINY-Lung01 will be presented as part of the 2020 American Society of Clinical Oncology (ASCO) Virtual Scientific Program.

“We are encouraged by the promising evidence of activity seen with Enhertu in patients with advanced lung cancer and a HER2 mutation,” Gilles Gallant, BPharm, PhD, FOPQ, senior vice president, global head, Oncology Development, Oncology R&D, Daiichi Sankyo, stated in the press release. “We look forward to working closely with the FDA on the potential for Enhertu to become the first HER2 directed therapy approved for non–small cell lung cancer.”

The designation marks the third breakthrough therapy designation the FDA has granted for trastuzumab deruxtecan. The ADC first received the designation in 2017 for HER2-positive breast cancer and recently, the FDA granted trastuzumab deruxtecan the designation for the treatment of patients with HER2-positive unresectable or metastatic gastric or

gastroesophageal junction (GEJ) adenocarcinoma who have received 2 or more prior regimens including trastuzumab (Herceptin). The designation is supported by findings from the phase 2 DESTINY-Gastric01 trial, the full results of which are scheduled to be presented on the 2020 ASCO Virtual Scientific Program.

Trastuzumab deruxtecan is currently approved by the FDA for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received ≥2 prior anti–HER2-based regimens in the metastatic setting. The approval is based on findings from the phase II DESTINY-Breast01 trial. In the study, trastuzumab deruxtecan induced a confirmed ORR of 60.3% per independent central review, including a 4.3% complete response rate, and a 56% partial response rate.[3]

References

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